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(54) Title: SUBSTITUTED BENZOPENTATHIEPINS, PROCESS THEREFOR AND INTERMEDIATES

(57) Abstract

Substituted benzopentathiepins, their preparation from 1, 2, 3-benzothiadiazoles and elemental sulfur, selected 1, 2, 3-benzothiadiazoles; the benzopentathiepins being useful as intermediates to 1, 2-benzenedithiols or as agricultural anti-viral and anti-fungal agents.

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TITLE

SUBSTITUTED BENZOPENTATHIEPINS, PROCESS THEREFOR AND INTERMEDIATES

CROSS-REFERENCE TO RELATED APPLICATION

This is a continuation-in-part of copending Application Serial No. 502,231 filed on June 8, 1983.

BACKGROUND OF THE INVENTION

This invention concerns substituted benzopentathiepins, intermediate 1,2,3-benzothiadiazoles and the process for making the former by reacting the latter with elemental sulfur.

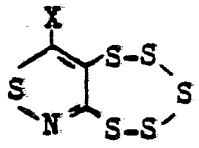
Unsubstituted benzopentathiepin is known (Feher et al., Z. Anorg. Allg. Chem., 452, 37 to 42 (1979); Feher et al., Tet. Lett., 2125 to 2126 (1971). It is prepared from 1,2-benzenedithiol and S_3Cl_2. No utility is described. Feher et al., in Z. Naturforsch. B, 27, 1006 (1972), describe preparation of the 7,8-dimethyl derivative by a similar method.

A reduced hexahydrobenzopentathiepin was prepared by Feher et al., according to the method of Feher et al. described above: Angew. Chem. Int. Ed., 6, 703 (1967). Nametkin et al., in Izv. Akad. Nauk. SSSR, Ser. Khim., 12, 2841 (1980), describe a method for making said reduced pentathiepins by use of an organoiron complex.

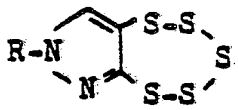
Watkins et al., J. Het. Chem., 19, 459 to 462 (1982) describe the x-ray crystal structure of a complex indene pentathiepin. Synthesis and utility are not described.

A variety of heterocyclic pentathiepins are known. For instance, U.S. 4,094,985 describes the

following as fungicides:

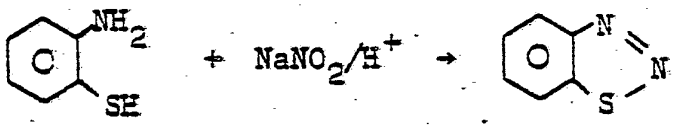


where X is CN or -CQ, et cetera. U.S. 4,275,073 describes these pyrazolopentathiepins as fungicides:



where R = H, C_1-C_6 alkyl, C_5-C_6 cycloalkyl, $-CH_2Ø$, -Ar. Both of the patents describe processes employing a thiol or dithiol and S_2Cl_2. The substituted benzopentathiepins of this invention cannot be made by literature techniques.

Certain 1,2,3-benzothiadiazoles are known, their syntheses being reviewed by Kurzer in "Org. Cmpd. of Sulphur, Selenium, Tellurium", Royal Society of Chemistry, London, Vols. 1 to 6 (1970 to 1980). A typical synthesis is diazotization of an o-aminobenzenethiol as follows:



In Oae, "Organic Chemistry of Sulfur", at pages 346 to 348, Plenum Press, N.Y. (1977), are reviewed the various means of reducing disulfides to give thiols. Reagents for these reductions include sodium borohydride, lithium aluminum hydride, sodium

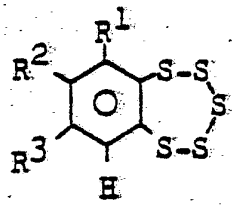
amalgam, zinc or tin with aqueous acid, phosphines and phosphites.

Cairns et al., J. Am. Chem. Soc., 74, 3982 to 3989 (1952), describe the reduction of a linear tetrasulfide by lithium aluminum hydride. There is no known art, however, that describes reduction of a pentathiepin to give a dithiol.

The 1,2-benzenedithiols can be prepared by pyrolysis of benzothiadiazoles in the presence of carbon disulfide and alkaline hydrolysis of the intermediate trithiocarbonate: Hunig et al., Liebigs Ann. Chem., 738, 192 to 194 (1970). The process requires a pressure vessel and temperatures of 220°C.

SUMMARY OF THE INVENTION

This invention concerns novel substituted benzopentathiepins of the formula:



wherein

R^1, R^2 and R^3 are the same or different substituents that do not react with sulfur at elevated temperatures and are selected from H (no more than two of R^1, R^2 and R^3 being H), X, CX_3, NO_2, SR^4, OR^4, NR^4_2, OCR^4 (O), COR^4 (O), CR^4 (O), CNR^4_2 (O), aryl and substituted aryl;

R^4 is selected from aryl, substituted aryl and substituted and unsubstituted branched or straight chain C_1 to C_6 alkyl; and

X is selected from Cl, Br and F.

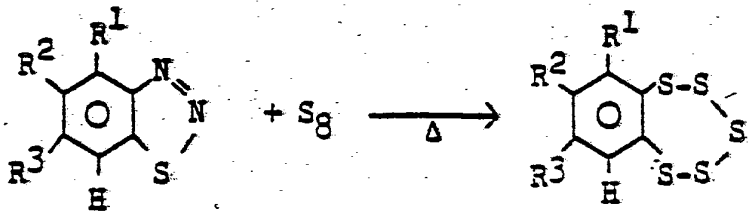
The primary requirement of the R^1, R^2 and R^3 substituents is that they be substantially

unreactive with sulfur at reaction temperatures. Several groups of such substituents are given as examples with no intent that the invention be limited thereto.

The substituents on substituted R^4 aryl and alkyl groups are selected from X, CX_3, OR, SR, OCR, and COOR, wherein R is aryl or C_1 to C_4

straight or branched alkyl. Preferred benzopentathiepins of this invention are those wherein: (1) R^1 and R^3 are both H and R^2 is selected from X, CX_3, SR^4, OR^4, NR^4_2, $COOR^4$, aryl and substituted aryl; (2) R^2 and R^3 are both H and R^1 is selected from X, CX_3, SR^4, OR^4, NR^4_2, $COOR^4$, aryl and substituted aryl; and (3) R^1 and R^2 are both NR^4_2 and R^3 is H. Especially preferred compounds are those in category (1) wherein R^2 is $N(CH_3)_2$, OCH_3, CF_3 or Cl; those in category (2) wherein R^1 is CF_3 or Br; and the compound in category (3) wherein R^4 is methyl. The latter compound is named 6,7 bis(dimethylamino)benzopentathiepin.

This invention also concerns the method for making benzopentathiepins by the following reaction:



The reaction is typically carried out in an inert solvent at temperatures between about 140° to 200°C, with about 160° to 190°C being preferred. The R^1,

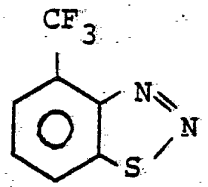
R^2 and R^3 substituents are as defined heretofore except that the novel process also includes the making of compounds wherein $R^1 = R^2 = R^3 = H$.

Suitable solvents are those which are inert to elemental sulfur and are tolerant of temperature and pressure combinations required to meet the temperature range described. The solvents include but are not limited to decahydronaphthalene, nitrobenzene, dichlorobenzenes, dimethylformamide and dimethyl sulfoxide. The reaction is normally carried out in an inert atmosphere such as nitrogen, argon, helium and the like. The molar ratio of elemental sulfur (calculated as S_8) to benzothiadiazole can range from about 1:2 to 2:1; the preferred ratio is about 1:1.

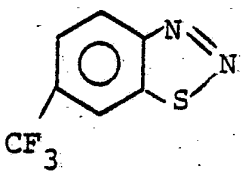
This invention also concerns the method for making said benzopentathiepins in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO):

The molar ratio of DABCO to benzothiadiazole is about 0.1:1 to 2:1; the preferred ratio is about 1:1. Employing DABCO in the process of the invention has been found to increase product yields substantially.

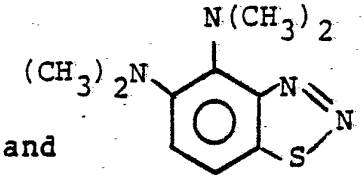
This invention also concerns these novel benzothiadiazoles:



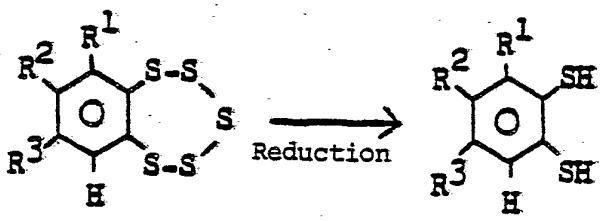
and



and



This invention also concerns the method for making substituted 1,2-benzenedithiols by reduction of benzopentathiepins according to the reaction:



wherein R^1, R^2 and R^3 are as defined above including $R^1 = R^2 = R^3 = H$.

Suitable reducing agents for said process include but are not limited to sodium borohydride, lithium aluminum hydride, trialkyl phosphites, zinc/aqueous acid, and the like. Sodium borohydride and lithim aluminum hydride are preferred. The reaction temperature can be about 0° to 60°C; the preferred range for sodium borohydride, for reasons of ease of reactivity, is about 20° to 40° C; the preferred range for lithium aluminum hydride is about 0° to 35°C.

DETAILS OF THE INVENTION

In the matter of making 1,2-benzenedithiols, the following information will guide one skilled in the art regarding choice of solvents. The process employing sodium borohydride is run with a protic solvent, with or without non-protic solvents as diluent. Solvents suitable for the sodium borohydride process include but are not limited to methanol, ethanol, isopropanol, butanol and water. Non-protic diluents include tetrahydrofuran. Other solvents can be selected empirically depending on the type of reducing agent selected. Thus, lithium aluminum hydride requires non-protic solvents such as diethyl ether or tetrahydrofuran.

The molar ratio of sodium borohydride or lithium aluminum hydride to benzopentathiepin can range from about 2:1 to 6:1; a ratio of about 4:1 is preferred. The process employing lithium aluminum hydride should be run in the absence of water. The reaction process initially gives a dithiolate salt which can be further reacted with aqueous acid to give the 1,2-benzenedithiols, or with alkylating agents such as methyl iodide to give di-thioethers. The second choice gives materials which are protected against aerobic oxidation.

An additional aspect of this invention concerns the use of selected benzopentathiepins as anti-fungal and anti-viral agents. For example, the compounds of Table 1 were found to be effective against the recited fungus and virus types. Details concerning formulations and control methodology follow the Table.

TABLE 1

Compound	Fungus or Virus[1]	Rate	% Control
7-Trifluoromethyl-benzopentathiepin	AS	100ppm	100
	RB	100ppm	90
7-Dimethylamino-benzopentathiepin	AS	100ppm	100
	CPM	100ppm	100
	CMV	100ppm	100
	BPM	100ppm	55
7-Methoxybenzo-pentathiepin	AS	100ppm	100
	CPM	100ppm	93
	BPM	100ppm	95
6-Trifluoromethyl benzopentathiepin	CPM	100ppm	100
6,7-bis(dimethylamino)-benzopentathiepin	AS	100ppm	80 (primary) 98 (confirmatory)
	WLR	100ppm	80 (primary) 57 (confirmatory)

(1) AS=apple scab
RB=rice blast
CPM=cucumber powdery mildew
BPM=barley powdery mildew
CMV=cucumber mosaic virus
WLR=wheat leaf rust

PLANT DISEASE CONTROL FORMULATIONS

Useful formulations of benzopentathiepins can be prepared in conventional ways. They include dusts, suspensions, emulsions, wettable powders, emulsifiable concentrates and the like. Many of them can be applied directly. Sprayable formulations can be extended in suitable media and used at spray

volumes of from a few liters to several hundred liters per hectare. High strength compositions can be used primarily as concentrates which are to be diluted prior to ultimate use. The formulations, broadly, contain about 1% to 99% by weight of active ingredient(s) and at least one of (a) about 0.1% to 20% surfactant(s) and (b) about 1% to 99% solid or liquid diluent(s). More specifically, they will contain these ingredients in the approximate proportions set forth in Table 2 with the active ingredient plus at least one surfactant or diluent being equal to 100 weight percent.

TABLE 2

	Weight Percent		
	Active Ingredient	Diluent(s)	Surfactant(s)
Wettable Powders	20-90	0-74	1-10
Oil Suspensions, Solutions	5-50	40-95	0-15
Emulsions (including Emulsifiable Concentrates)			
Aqueous Suspensions	10-50	40-84	1-20
Dusts	1-25	70-99	0-5
High Strength Compositions	90-99	0-10	0-2

Lower or higher levels of active ingredient can be present, depending on the intended use and the physical properties of the compound. Higher ratios of surfactant to active ingredient are sometimes desirable and are achieved by incorporation into the formulation, or by tank mixing.

Some typical solid diluents are described in Watkins et al., "Handbook of Insecticide Dust Diluents and Carriers", 2nd Ed., Dorland Books.

Caldwell, N.J. but other solids, either mined or manufactured, can be used. The more absorptive diluents are preferred for wettable powders and the denser ones for dusts. Typical liquid diluents and solvents are described in Marsden, "Solvents Guide", 2nd Ed., Interscience, N.Y., 1950. Solubility under 0.1% is preferred for suspension concentrates; solution concentrates are preferably stable against phase separation at 0°C. "McCutcheon's Detergents and Emulsifiers Annual", MC Publishing Corp., Ridgewood, N.J., as well as Sisely and Wood, "Encyclopedia of Surface Active Agents", Chemical Publishing Co., Inc., N.Y., 1964, list surfactants and recommended uses. All formulations can contain minor amounts of additives to reduce foaming, caking, corrosion, microbiological growth, and the like.

Agricultural formulations that contain the compounds of this invention as active ingredient can also contain other active ingredients. The additional agricultural chemicals are employed in mixtures or combinations in amounts ranging from 0.05 to 25 parts by weight for each part by weight of the compound or compounds of this invention. The proper choice of amounts is readily made by one skilled in the art of protecting plants from pests. The following are illustrative of the agricultural chemicals that can be included in compositions or added to sprays containing one or more of the active compounds of this invention:

Fungicides:

methyl 2-benzimidazolecarbamate (carbendazim)
tetramethylthiuram disulfide (thiuram)
n-dodecylguanidine acetate (dodine)
manganese ethylenebisdithiocarbamate (maneb)
1,4-dichloro-2,5-dimethoxybenzene (chloroneb)

methyl 1-(butylcarbamoyl)-2-benzimidazolecarbamate (benomyl)

2-cyano-N-ethylcarbamoyl-2-methoxyiminoacetamide (cymoxanil)

N-trichloromethylthiotetrahydrophthalimide (captan)

N-trichloromethylthiophthalimide (folpet)

dimethyl 4,4'-(o-phenylene)bis(3-thioallophanate) (thiophanate-methyl)

2-(thiazol-4-yl)benzimidazole (thiabendazole)

aluminum tris(O-ethyl phosphonate) (Aliette®)

tetrachloroisophthalonitrile (chlorothalonil)

2,6-dichloro-4-nitroaniline (dichloran)

N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine methyl ester (metalaxyl)

cis-N-[(1,1,2,2-tetrachloroethyl)thio] cyclohex-4-ene-1,2-dicarbioximide (captafol)

3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidine carboxamide (iprodione)

3-(3,5-dichlorophenyl)-5-ethenyl-5-methyl-2,4-oxazolidinedione (vinclozolin)

kasugamycin

O-ethyl-S,S-diphenylphosphorodithioate (edifenphos)

Bactericides:

tribasic copper sulfate

streptomycin sulfate

oxytetracycline

Acaricides:

senecioic acid, ester with 2-sec-butyl-4,6-dinitrophenol (binapacryl)

6-methyl-1,3-dithiolo [2,3-B] quinonolin-2-one (oxythioquinox)

2,2,2-trichloro-1,1-bis(4-chlorophenyl)ethanol (dicofol)

bis(pentachloro-2,4-cyclopentadien-1-yl) (dienochlor)

tricyclohexyltin hydroxide (cyhexatin)

hexakis(2-methyl-2-phenylpropyl)distannoxane (fenbutin oxide)

Nematicides:

2-[diethoxyphosphinylimino]-1,3-dithietane (fosthietan)

S-methyl-1-(dimethylcarbamoyl)-N-(methyl-carbamoyloxy)thioformimidate (oxamoyl)

S-methyl-1-carbamoyl-N-(methylcarbamoyloxy)-thioformimidate

N-isopropylphosphoramidic acid, O-ethyl-O'-[4-(methylthio)-m-tolyl] diester (fenamiphos)

Insecticides:

3-hydroxy-N-methylcrotonamide(dimethylphosphate)-ester (monocrotophos)

methylcarbamic acid, ester with 2,3-dihydro-2,2-dimethyl-7-benzofuranol (carbofuran)

O-[2,4,5-trichloro-α-(chloromethyl)benzyl] phosphoric acid, O',O,-dimethyl ester (tetrachlorvinphos)

2-mercaptosuccinic acid, diethyl ester, S-ester with thionophosphoric acid, dimethyl ester (malathion)

phosphorothioic acid, O,O-dimethyl, O-p-nitrophenyl ester (methyl parathion)

methylcarbamic acid, ester with α-naphthol (carbaryl)

methyl N-[[(methylamino)carbonyl]oxy] ethanimidothioate (methomyl)

N'-(4-chloro-o-tolyl)-N,N-dimethylformamidine (chloridimeform)

O,O-diethyl-O-(2-isopropyl-4-methyl-6-pyrimidyl) phosphorothioate (diazinon)

octachlorocamphene (toxaphene)

O-ethyl O-p-nitrophenyl phenylphosphononthioate (EPN)

cyano(3-phenoxyphenyl)-methyl 4-chloro-α-(1-methylethyl)benzeneacetate (fenvalerate)

(3-phenoxyphenyl)methyl (+)-cis,trans-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane-carboxylate (permethrin)

dimethyl N,N'-[thiobis](N-methylimino)carbonyl-oxy]]-bis[ethanimidothioate] (thiodicarb)

phosphorothiolothionic acid, O-ethyl-O-[4-(methylthio)phenyl]-S-n-propyl ester (sulprofos)

α-cyano-3-phenoxybenzyl[3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane]carboxylate (cypermethrin)

cyano(3-phenoxyphenyl)methyl 4-(difluoromethoxy-α-(methylethyl)benzeneacetate (Payoff®)

O,O-diethyl-O-(3,5,6-trichloro-2-pyridyl)-phoshorothioate (chlorpyrifos)

O,O-dimethyl-S-[(4-oxo-1,2,3-benzotriazin-3-(4H)-yl)-methyl]phosphorodithioate (azinphos-methyl)

5,6-dimethyl-2-dimethylamino-4-pyrimidinyl dimethyl carbamate (Pirimor®)

S-(N-formyl-N-methylcarbamoylmethyl)-O,O-dimethyl phosphorodithioate (formothion)

S-2-(ethylthioethyl)-O,O-dimethyl phosphiorothioate (demeton-S-methyl)

α-cyano-3-phenoxybenzyl cis-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxylate (deltamethrin)

cyano(3-phenoxyphenyl)methyl ester of N-(2-chloro-4-trifluoromethylphenyl)alanine (Mavrik®).

The methods for making such compositions are well known. Solutions are prepared by simply mixing the ingredients. Fine solid compositions are made by blending and, usually, grinding as in a hammer or fluid energy mill. Suspensions are prepared by wet milling. Granules and pellets can be made by spraying the active material on preformed granular carriers or by agglomeration techniques.

Disease control is accomplished by applying the compounds of this invention to the portion of the plant to be protected. The compounds can be applied as preventive treatments prior to inoculation with the pathogen, or after inoculation as a curative post-infection treatment.

Rates of application for compounds of this invention will be influenced by specific host plants, fungal pathogens, and many factors of the environment must be determined under use conditions. Foliage sprayed with concentrations ranging from 1 to 500 ppm of active ingredient can be protected from disease under suitable conditions.

The "% Control" in Table 1 was calculated according to this formula:

$$100 - \left[\frac{\text{disease rating on treated plants}}{\text{disease rating on untreated plants}} \times 100 \right] = \text{percent control}$$

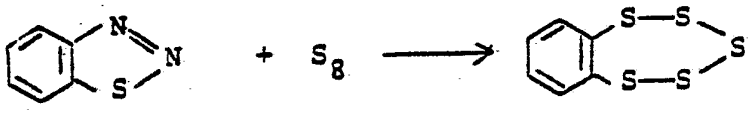
The benzopentathiepins of this invention have generic utility as intermediates in the preparation of substituted 1,2-benzenedithiols which are free of the 1,3-and 1,4-dithiol isomers. Such substituted 1,2-benzenedithiols are known intermediates to pharmaceuticals (U.S. 4,242,510; Sindelar et al., Collect. Czech. Chem. Comm., 47, 72 to 87 (1982), pesticides (U.S. 3,746,707), and rubber crosslinking agents (U.S. 3,979,369).

Reduction of the benzopentathiepins with, for example, sodium borohydride gives solutions of disodium benzene dithiolates which can be neutralized to give the dithiol or alkylated with methyl iodide to give 1,2-bis(alkylthio)benzene derivatives. It would be possible to react the dithiolates with anhydrides; acid halides; esters; isocyanates; sulfonyl halides; tri- and pentavalent phosphorous esters, halides and anhydrides to make other useful materials.

In the following Examples the inert atmosphere was N_2. Kugelrohr distillation refers to a bulb-to-bulb microdistillation assembly. Examples 1 to 7 and 16 illustrate the process of the invention for preparation of benzopentathiepins. Examples 2 to 7 and 16 illustrate novel benzopentathiepins. Examples 8 to 10 illustrate the yield enhancement of the process by employing DABCO. Examples 11, 12 and 15 illustrate the novel benzothiadiazole compounds. Examples 13 and 14 illustrate the process for conversion of benzopentathiepins to dithiols. In both Examples 13 and 14, the dithiols obtained are isolated as bismethylthioethers to prevent aerobic oxidation. These bismethylthioethers can be converted back to the benzenedithiols by treatment with, for example, sodium in liquid ammonia.

EXAMPLE 1

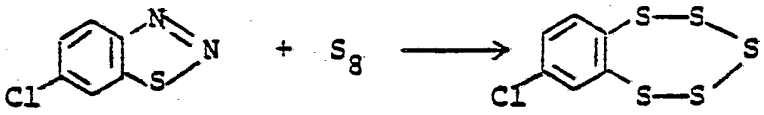
Benzopentathiepin



Sulfur (1.88 g, 7.3 mmol), 1,2,3-benzothiadiazole (1.0 g, 7.3 mmol) and Decalin®, i.e., decahydronaphthalene (10 mL) were combined and heated to 170°C for 1.45 h. The resulting mixture was taken up in carbon disulfide and chromatographed on Silica Woelm® TSC (250 g, hexane). After a 340 mL forerun, 50 mL fractions were taken. Fractions 4 to 16 contained 1.61 g of oily solid. This residue was triturated with hexane (30 mL) while methylene chloride (15 mL) was added slowly. Sulfur, 0.47 g was left as residue. The yellow solution was purified in 3x15 mL portions by medium pressure liquid chromatography (MPLC) (Lobar® Silica gel 60 size C, hexane) to give 0.60 g (34%) of benzopentathiepin as a light yellow solid, mp 56° to 58°C. A sample recrystallized once from hexane had a mp of 58° to 60°C; ^{1}H-NMR($CDCl_3$, 90 MHz) δ 7.85-7.7 and 7.45-7.2 (AA'BB' multiplet) in agreement with the literature. The mass spectrum from a sample prepared similarly but not purified by MPLC had Mass spec.: m/e 235.8914; calcd m/e for $C_6H_4S_5$ 235.8917.

EXAMPLE 2

7-Chlorobenzopentathiepin



A mixture of sulfur (4.5 g, 17.6 mmol), 6-chloro-1,2,3-benzothiadiazole (3.0 g, 17.6 mmol) and Decalin® (12 mL) was heated to 170°C for 1 h and nitrogen evolved steadily. The mixture was then heated to 180°C for 1 h. The solution was cooled and

the solvent was removed in a stream of nitrogen overnight. The yellow residue was dissolved in carbon disulfide and absorbed onto Silica Woelm® TSC (20 g) and chromatographed on 250 g of the same silica (hexane eluent). After a 300 mL forerun, sulfur and residual decalin were eluted in 100 mL, then 4.59 g of sulfur and product were obtained in 750 mL. A 0.3 g sample was partially dissolved in hexane (10 mL) with stirring and portionwise addition of methylene chloride (10 mL). After 10 min, 0.07 g sulfur was decanted. The solution was purified by medium pressure liquid chromatography (Lobar® Silica gel 60, size C, hexane eluent) to give 0.07 g of 7-chlorobenzopentathiepin corresponding to a 22.5% yield. A 0.05 g sample was recrystallized from boiling hexane (20 mL concentrated to 5 mL, cooling and seeding) to give 40 mg of off-white solid, mp 87.5° to 89°C. A sample from a similar preparation had ^{1}H-NMR ($CDCl_3$, 80 MHz) δ 7.9-7.7 (d, 2H), 7.4-7.2 (m, 1H); IR (KBr) 1095, 822 cm^{-1}; Mass spec.: m/e 269.8517; m/e calcd for $C_6H_3ClS_5$ 269.8527.

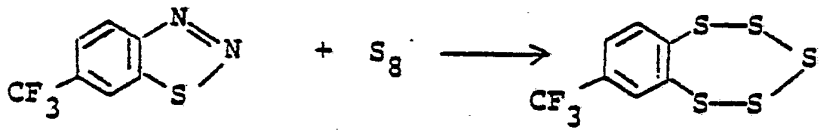
Anal. Calcd for $C_6H_3ClS_5$: C, 26.61; H, 1.12, S, 59.19.

Found: C, 26.84; H, 1.22; S, 65.7, 56.01, 56.79

The difference between the calculated and found values for sulfur was ascribed to a temporary difficulty with the analysis.

EXAMPLE 3

7-Trifluoromethylbenzopentathiepin



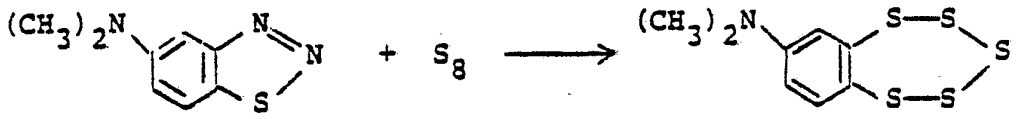
A mixture of sulfur (1.34 g, 4.9 mmol), 6-trifluoromethyl-1,2,3-benzothiadiazole (1.0 g, 4.9 mmol) and Decalin® (10 mL) was heated to 190°C for 45 min while nitrogen evolved. The mixture was cooled and stored overnight, then it was preadsorbed and chromatographed on Silica Woelm® TSC (400 g, hexane) to give 1.36 g of a sulfur-product mixture. This mixture was triturated with hexane (40 mL), decanting from sulfur. The solution was purified by medium pressure liquid chromatography (Lobar® Silica gel 60, size C) in 2 portions to give 0.46 g, 31% of 7-trifluoromethylbenzopentathiepin as a yellow oil which solidified on standing. A sample prepared by a similar procedure melted at 44° to 50°C. A sample recrystallized from hexane had mp 59° to 60°C; ^{1}H-NMR ($CDCl_3$) δ 8.18 (d, J=2Hz, 1H), 8.0 (d, J=8Hz, 1H), 7.55 (dd, J=2, 8Hz, 1H); IR(KBr) 1320 cm^{-1}; Mass spec.: m/e 303.8788; calcd m/e for $C_7H_3F_3S_5$ 303.8790.

Anal. calcd for $C_7H_3F_3S_5$: C, 27.62; H, 0.99; S, 52.66.

Found: C, 27.92; H, 0.94; S, 51.75
C, 28.14; H, 1.10; S, 51.98

EXAMPLE 4

7-Dimethylaminobenzopentathiepin



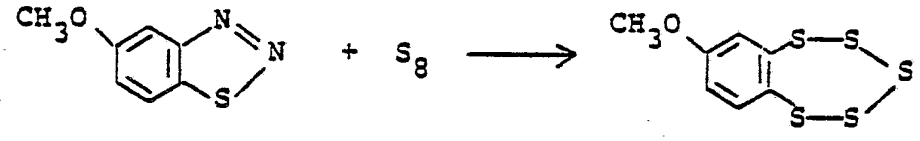
A mixture of sulfur (0.72 g, 2.79 mmol), 5-dimethylamino-1,2,3-benzothiadiazole (0.5 g, 2.79 mmol) and Decalin® (5 mL) was heated to 170°C for 1.5 h with steady evolution of nitrogen. The solution was cooled and the Decalin® was removed by Kugelrohr distillation at 50°C (0.3 mm). The residue was preadsorbed (5 g) and chromatographed (100 g) on Silica Woelm® TSC (1% ether-hexane) giving first sulfur and then 0.32 g (40%) of 7-dimethylaminobenzo pentathiepin, mp 115° to 118°C; ^{1}H-NMR ($CDCl_3$, 80 MHz) δ 7.55 (d, J=8.5 Hz, 1H), 7.0 (d, J=2.7Hz, 1H), 6.5 (dd, J=8.5,2.7Hz, 1H), 3.0 (s, 6H); IR(KBr)1583 cm^{-1}; Mass spec.: m/e 278.9343, calcd m/e for $C_8H_9NS_5$ 278.9338. An 80 mg sample was recrystallized from boiling ethanol (50 mL filtered and concentrated to 20 mL) to give 70 mg of bright yellow crystals, mp 121.5° to 122.5°C.

Anal. calcd for $C_8H_9NS_5$: C,34.38; H, 3.25; S, 57.36.

Found: C, 34.21; H, 3.42; S, 56.99.

EXAMPLE 5

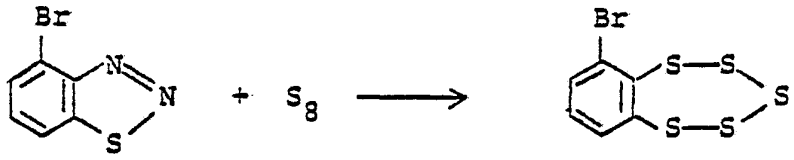
7-Methoxybenzopentathiepin



A mixture of sulfur (0.77 g, 3.01 mmol), 5-methoxy-1,2,3-benzothiadiazole (0.5 g, 3.01 mmol) and Decalin® (5 mL) was heated to 170°C for 1.5 h. The solution was cooled and the Decalin® was removed by Kugelrohr distillation at 50°C (0.3 mm). The residue was preadsorbed (5 g) and chromatographed (100 g) on Silica Woelm® TSC (1% ether-hexane) to give first sulfur and then 0.27 g of 7-methoxybenzopentathiepin as a light yellow solid, mp 90° to 95°C. The sample was further purified by high pressure liquid chromatography (Zorbax® Sil, 25% methylene chloride-hexane) to give 0.17 g, 21% of the product, mp 97° to 98°C; IR(KBr) 1577, 1291, 1229, 1037 cm^{-1}; Mass spec.: m/e 265.9011, m/e calcd for $C_7H_6OS_5$ 265.9022. A sample prepared by a similar procedure had ^{1}H-NMR ($CDCl_3$, 80 MHz) δ 7.75 (d, J=8.3Hz, 1H), 7.3 (d, J=2.7Hz, 1H), 6.8 (dd, J=2.7, 8.3Hz, 1H), 3.85 (s, 3H).

EXAMPLE 6

6-Bromobenzopentathiepin



A mixture of sulfur (2.4 g, 9.3 mmol), 4-bromo-1,2,3-benzothiadizole (2.0 g, 9.3 mmol) and Decalin® (20 mL) was heated to 175°C for 1.25 h and nitrogen was evolved. The mixture was cooled and the solvent was removed by Kugelrohr distillation. The residue was preadsorbed and chromatographed (300 g) on Silica Woelm® TSC (1% ether-hexane) to give first sulfur and then 2.2 g of a sulfur-product mixture. The mixture was purified by high pressure liquid chromatography (Zorbax® Sil, hexane) to give 0.43 g, 14.6% of 6-bromobenzopentathiepin, retention time = 5.12 min, mp 93° to 98°C; IR(KBr) 788 cm^{-1}; Mass spec.: m/e 313.8036, m/e calcd for $C_6H_3BrS_5$ 313.8021.

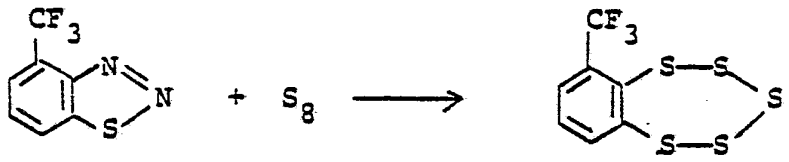
A compound prepared similarly and recrystallized from hexane had a mp of 101° to 101.5°C; NMR ($CDCl_3$, 360 MHz) δ 7.78 (dd, J=1.3, 8.0 Hz, 1H) 7.66 (dd, J=1.3, 8.0Hz, 1H) 7.12 (t, J=8.0Hz, 1H).

Anal. calcd for $C_6H_3BrS_5$: C=22.86; H=0.96

Found: C=23.53; H, 1.04
C=23.09; H, 0.94.

EXAMPLE 7

6-Trifluoromethylbenzopentathiepin

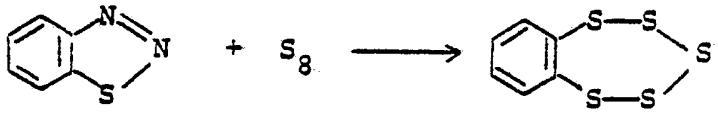


A mixture of sulfur (0.65 g, 2.45 mmol), 4-trifluoromethyl-1,2,3-benzothiadiazole (0.5 g, 2.45 mmol) and Decalin® (5 mL) was heated to 180°C for 3 h and nitrogen was slowly evolved. The mixture was cooled and the solvent was removed by Kugelrohr distillation. The residue was preadsorbed and chromatographed (100 g) on Silica Woelm® TSC (1% ether-hexane) giving first sulfur and then 0.55 g of a sulfur-product mixture. The mixture was purified by high pressure liquid chomatography (Zorbax® Sil, hexane) to give 0.15 g, 20% of 6-trifluoromethylbenzopentathiepin as a light yellow solid, mp 55° to 60°C, retention time = 5.26 min, IR(KBr) 1310, 1137, 1129, 1119 cm^{-1}; Mass spec.: m/e 303.8748, m/e calcd for $C_7H_3F_3S_5$ 303.8791. A compound prepared similarly and recrystallized from hexane had a mp of 61° to 62°C.

Anal. Calcd for $C_7H_3F_3S_5$: C=27.62; H=0.99

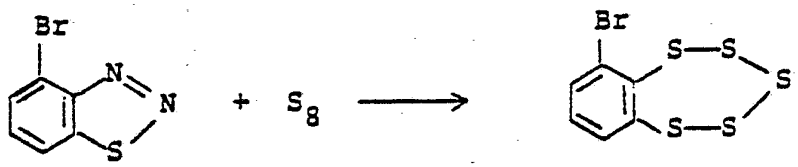
Found: C, 27.89; H, 1.06
C, 27.65; H, 1.03.

EXAMPLE 8



A mixture of sulfur (1.88 g, 7.3 mmol), 1,2,3-benzothiadiazole (1.0 g, 7.3 mmol), 1,4-diazabicyclo[2.2.2]octane (0.82 g, 7.3 mmol) and Decalin® (10 mL) was heated to 170°C for 1.5 h while nitrogen was evolved. The mixture was cooled and the solvent was removed by Kugelrohr distillation. The residue was chromatographed on Silica Woelm® TSC (200 g, 1% ether-hexane). The fraction containing the product was further purified by high pressure liquid chromatography to give 0.94 g, 54%, of benzopentathiepin.

EXAMPLE 9



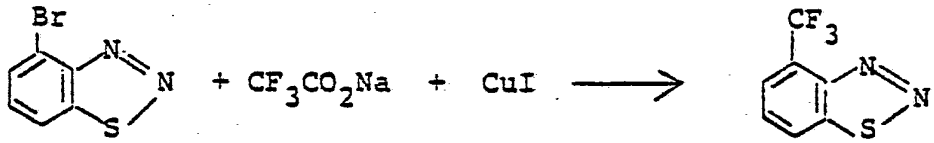
A mixture of sulfur (1.2 g, 4.65 mmol), 4-bromo-1,2,3-benzothiadiazole (1.0 g, 4.65 mmol), 1,4-diazacyclo[2.2.2]octane (0.52 g, 4.65 mmol), and Decalin® (10 mL) was heated at 170°C for 1.25 h. The mixture was cooled and the solvent was removed by Kugelrohr distillation. The residue was chromatographed on Silica Woelm® TSC (200 g, 1% ether-hexane). The fraction containing a sulfur-product mixture was further purified by high pressure liquid chromatography (Zorbax® Sil, hexane) to give 0.33 g, 22.6%, of 6-bromobenzopentathiepin.

EXAMPLE 10

A mixture of sulfur (0.77 g, 3.01 mmol), 5-methoxy-1,2,3-benzothiadiazole (0.5 g, 3.01 mmol), 1,4-diazabicyclo[2.2.2]octane (0.34 g, 3.01 mmol) and Decalin® (5 mL) was heated to 170°C for 1.25 h. The mixture was cooled and the solvent was removed by Kugelrohr distillation. The residue was chromatographed on Silica Woelm® TSC (200 g, 1% ether-hexane) to give first sulfur and then 0.46 g, 57%, of 7-methoxybenzopentathiepin.

EXAMPLE 11

4-Trifluoromethyl-1,2,3-Benzothiadiazole



First, 4-bromo-1,2,3-benzothiadiazole (5.0 g, 23.2 mmol) was dissolved in N-methylpyrrolidinone (200 mL) and then sodium trifluoroacetate (8.5 g, 62.5 mmol) and cuprous iodide (8.75 g, 46 mmol) were added. The mixture was heated to 160°C for 4 h (gentle CO_2 evolution), cooled, and diluted carefully with water (300 mL). The slurry was filtered through Celite® (diatomaceous earth) and the pad was rinsed with ether (3x250 mL). The filtrate phases were separated and the organic layer was washed with water and brine; then it was filtered

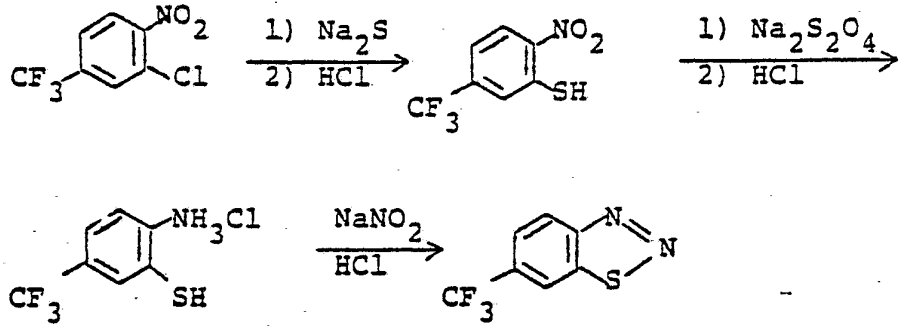
through a cone of calcium sulfate and concentrated. The crude product was chromatographed on Silica Woelm® TSC (500 g, 15% ether-hexane) to give first a mixture of 4-bromo and 4-iodo and 4-trifluoromethyl-1,2,3-benzothiadiazoles followed by pure 4-trifluoromethyl-1,2,3-benzothiadiazole. The mixed fraction was rechromatographed on the same column to give additional pure product. In this manner, 3.19 g, 67%, of 4-trifluoromethyl-1,2,3-benzothiadiazole was obtained as an off-white solid. A sample prepared by a similar procedure had mp 41° to 44°C; ^{19}F NMR ($CDCl_3$) -58.78 (s). A sample further purified by sublimation at 45°C (35-50 mm-water aspirator) had mp 49° to 51°C; ^1H-NMR ($CDCl_3$) δ 8.35 (d, J=8Hz, 1H), 8.0 (d, J=8Hz, 1H), 7.8 (t, J=8Hz, 1H); IR(KBr) 1319, 1152, 1122, 1089 cm^{-1}.

Anal. calcd for $C_7H_3F_3N_2S$: C, 41.18; H, 1.48; N,13.72.

Found: C, 41.13; H, 1.37; N, 13.96.

EXAMPLE 12

6-Trifluoromethyl-1,2,3-Benzothiadiazole



First, 2-chloro-4-trifluoromethylnitrobenzene (20 g, 88.6 mmol) was dissolved in dimethylsulfoxide (100 mL, dried over molecular sieves) under a nitrogen atmosphere and then

anhydrous sodium sulfide (6.92 g, 88.6 mmol) was added all at once. The mixture warmed to about 40°C and was stirred for 2 h. The red mixture was poured into a solution of brine (300 mL) and 6N HCl (100 mL) and extracted with methylene chloride (3x100 mL). The combined organic phase was filtered through a cone of sodium sulfate and concentrated to leave 18.46 g of yellow solid.

Nitrogen was bubbled through deionized water (400 mL) for 15 min, then the above yellow solid and ammonium hydroxide (90 mL) were added. Sodium hydrosulfite (90 g) was dissolved in deionized water (400 mL) and added to the mechanically stirred reaction over 10 to 15 min via an addition funnel. The resulting solution was warmed to 50°C for 3 h, then stirred overnight at ambient temperature. The mixture was acidified to pH 7 with acetic acid and extracted with ether (3x200 mL). The combined organic layer was washed with brine and filtered through a cone of calcium sulfate into a flask equipped with mechanical stirring and a gas inlet. Hydrogen chloride was bubbled through the stirred solution for 1.5 h. The solid was filtered, rinsed with dry ether and dried <u>in vacuo</u> to give 8.96 g of hydrochloride salt, mp 184° to 188°C; IR (KBr) 1330 cm^{-1}.

The above salt was slurried in 5% aqueous HCl (100 mL) and chilled to 0°C. A solution of sodium nitrite (3.22 g) in water (15 mL) was added dropwise over 20 min to the stirred mixture; then it was neutralized to pH 9 with 20% aqueous sodium hydroxide. The reaction was extracted with ether (3 x100 mL) and the organic phase was washed with water and brine and then filtered through a cone of sodium sulfate. Concentration left 6.94 g of a brown

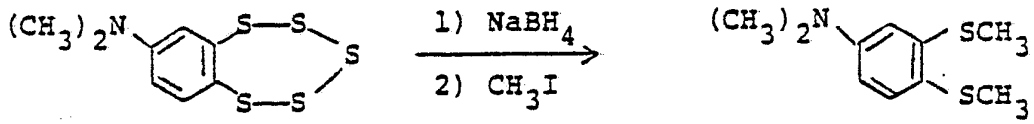
oil which was chromatographed on Silica Woelm® TSC (250 g, 10% ether-hexane) to give (after a 350 mL forerun) a trace of impurity in 250 mL and then 2.35 g of 6-trifluoromethyl-1,2,3-benzothiadiazole in 150 mL of eluent. A sample sublimed at 25°C (0.15 mm) had mp 36° to 40°C; ^{1}H-NMR ($CDCl_3$, 90 MHz) δ 8.9 (m, 1H), 8.25 (dd, 1H), 7.9 (ddd, 1H); IR (KBr) 1332, 1294, 1192, 1150, (sh) 1129 cm^{-1}. A sample prepared by a similar procedure had mp 40° to 42°C.

Anal. calcd for $C_7H_3F_3N_2S$: C, 41.18; H, 1.48; N, 13.72.

Found: C, 41.31; H, 1.51; N, 13.56.
40.95 1.73 13.82.

EXAMPLE 13

3,4-Bis(methylthio)-N-N-dimethylaniline



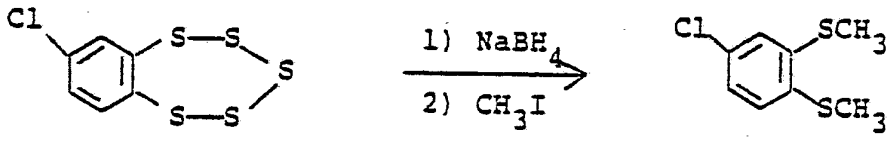
This Example illustrates the making of a compound useful (as the unprotected dithiol) as a rubber cross-linking agent. First, 7-dimethylaminobenzopentathiepin (0.5 g, 1.79 mmol) was dissolved in tetrahydrofuran (50 mL) and ethanol (50 mL) was added. Sodium borohydride (0.34 g, 8.96 mmol) was added to the stirred solution at ambient temperature over 5 min (after a short induction time hydrogen gas was evolved and the solution warmed slightly). When the foaming ceased in about 15 min, water (10 mL) was added and the mixture was warmed to 50°C for 5 min followed by cooling to ambient temperature and addition of methyl iodide (0.62 mL,

10 mmol). After stirring 30 min more, the solvent was removed and the residue was partitioned between water and ether. The phases were separated and the organic phase was washed with brine and dried through a cone of sodium sulfate. Concentration gave a yellow oil which was chromatographed on Silica Woelm® TSC (50 g, 20% ether-hexane) to give 0.33 g, 86%, of 3,4-bis(methylthio)-N,N-dimethylaniline as a yellow oil which crystallized on standing, mp 49° to 51°C; IR (neat) 1583 cm^{-1}; ^1H-NMR ($CDCl_3$, 80 MHz) δ 7.22 (d, J=9.3 Hz, 1H), 6.49 (d, partially obscured, J=2.9Hz, 1H), 6.4 (dd, partially obscured, J=2.9, 9.3 Hz, 1H), 2.95 (s, 6H), 2.46 (s, 3H), 2.38 (s, 3H).

Anal. calcd for $C_{10}H_{15}NS_2$: C, 56.30; H, 7.09.
Found: C, 56.69; H, 6.93.
C, 56.72; H, 6.96.

EXAMPLE 14

3,4-Bis(methylthio)-chlorobenzene

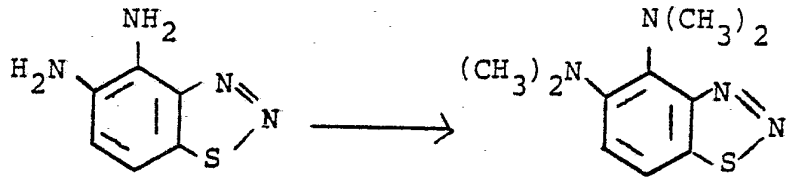


This Example illustrates the making of a compound useful as an intermediate (as the unprotected dithiol) to a tricyclic psychotropic agent. First, 7-chlorobenzopentathiepin (0.32 g, 1.18 mmol) was dissolved in tetrahydrofuran (30 mL) and ethanol (30 mL) was added. Sodium borohydride (0.22 g, 5.91 mmol) was added over 5 min in portions at ambient temperature causing the solution to evolve hydrogen gas and warm slightly. After gas evolution had ceased in about 15 min, water (10 mL) was added and the

mixture was heated to about 50°C for 5 min and cooled to ambient temperature. Methyl iodide (0.44 mL, 7.0 mmol) was added and the solution was stirred. The solvents were removed and the residue was partitioned between ether and water. The phases were separated and the organic layer was washed with brine and dried through a cone of sodium sulfate. Concentration left an oil which was chromatographed on Silica Woelm® TSC (50 g, 10% ether-hexane) to give 0.16 g, 67%, of 3,4-bis(methylthio)chlorobenzene as a clear pale yellow oil; ^{1}H-NMR ($CDCl_3$, 90 MHz) δ 7.1 (s, 3H), 2.46 (s, 3H), 2.44 (s, 3H), 1.4 (small impurity); IR (neat) 1448, 1430, 1029, 801 cm^{-1}; Mass spec.: m/e 203.9852, m/e calcd for $C_8H_9ClS_2$ 203.9834.

EXAMPLE 15

4,5-Bis(dimethylamino)-1,2,3-benzothiadiazole

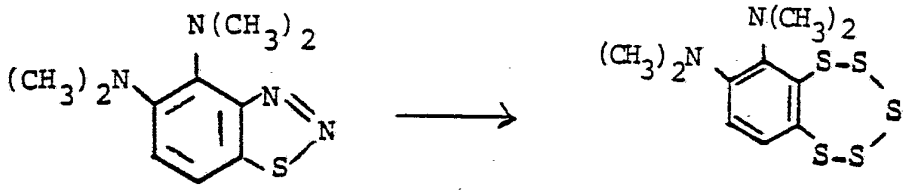


A 3 necked round bottom flask fitted with magnetic stirrer, condenser, static nitrogen atmosphere and a septum was charged with sodium hydride (0.35 g, 50% mineral oil dispersion, 7.2 mmol). The oil was rinsed away with dry hexane (3 times using standard syringe technique) then dry tetrahydrofuran (20 mL) was added. To the slurry was added 4,5-diamino-1,2,3-benzothiadiazole (0.2 g, 1.2 mmol) neat over 5 min. Finally, methyl iodide (0.75 mL, 12 mmol) was added and the mixture was stirred at ambient temperature for 72 h. The mixture

was cautiously quenched with water, the solvent was stripped off, and methylene chloride was added to the residue. After extraction of this organic phase with water and brine, it was filtered through a cone of sodium sulfate and concentrated onto silica gel. Chromatography on silica gel (5% ether-hexane) gave 0.11 g (41%) of 4,5-bis(dimethylamino)-1,2,3-benzothiadiazole as an orange oil: NMR (90 MHZ) δ 7.38 (ABq $\Delta\nu_{1-3}$ = 18 Hz, J = 8Hz, 2H), 3.26 (s, 6H), 2.8 (s, 6H); IR (neat) 2980-2780 (multiplet, m) 1542, 1495 cm^{-1}; exact mass calcd for $C_{10}H_{14}N_4S$; M/e 222.0939, observed M/e 222.0950.

EXAMPLE 16

6,7-Bis(dimethylamino)benzopentathiepin



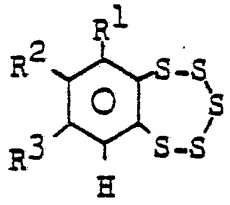
A magnetically stirred mixture of 4,5-bis(dimethylamino)-1,2,3-benzothiadiazole (2.0 g, 9.0 mmol), sulfur (2.3 g, 9.0 mmol) and decalin (30 mL) was heated to 175°C under a static nitrogen atmosphere for 1.5 h. During this time, nitrogen-evolution was steady. The mixture was cooled to ambient temperature and the decalin was removed by kugelrohr distillation. The residue was chromatographed on silica gel (1% ether-hexane) to give 2.04 g (70%) of 6,7-bis(dimethylamino)benzo-pentathiepin. A 1 g sample was recrystallized from 100 mL of hexane by chilling to -78°C to give 0.7 g of bright orange solid: mp 59.5° to 61°C. Anal. Calcd for $C_{10}H_{14}N_2S_5$; C, 37.24; H, 4.38;

Found: C, 37.45; H, 4.66. A sample prepared by a similar procedure had: NMR (80 mHz) δ 7.15 (ABq $\Delta\nu_{1-3}$ = 59 Hz, J = 8.5Hz, 2H), 2.9 (s, 6H), 2.8 (s, 6H).

CLAIMS:

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. A benzopentathiepin compound of the formula



wherein

R^1, R^2 and R^3 are the same or different and are selected from H (provided no more than two of R^1, R^2 and R^3 are H), X, CX_3, NO_2, SR^4, OR^4, NR^4_2, OCR^4, COR^4, CR^4, CNR^4_2, aryl and substituted aryl; R^4 is selected from aryl, substituted aryl, and substituted and unsubstituted branched or straight chain C_1 to C_6 alkyl; and

X is selected from Cl, Br and F.

2. A compound according to Claim 1 wherein R^1 and R^3 are both H and R^2 is selected from X, CX_3, SR^4, OR^4, NR^4_2, $COOR^4$, aryl and substituted aryl.

3. A compound according to Claim 2 wherein R^2 is selected from $N(CH_3)_2$, OCH_3, CF_3, and Cl.

4. A compound according to Claim 1 wherein R^2 and R^3 are both H and R^1 is selected from X, CX_3, SR^4, OR^4, NR^4_2, $COOR^4$, aryl and substituted aryl.

5. A compound according to Claim 4 wherein R^1 is selected from CF_3 and Br.

6. A compound according to Claim 3, 7-trifluoromethylbenzopentathiepin.

7. A compound according to Claim 3, 7-dimethylaminobenzopentathiepin.

8. A compound according to Claim 3, 7-methoxybenzopentathiepin.

9. A compound according to Claim 5, 6-trifluoromethylbenzopentathiepin.

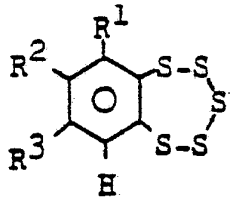
10. A compound according to Claim 3, 7-chlorobenzopentathiepin.

11. A compound according to Claim 5, 6-bromobenzopentathiepin.

12. A compound, 4-trifluoromethyl-1,2,3-benzothiadiazole.

13. A compound, 6-trifluoromethyl-1,2,3-benzothiadiazole.

14. A method for making compounds of the formula

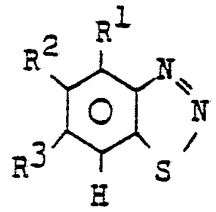


wherein

R^1, R^2 and R^3 are the same or different and are selected from H, X, CX_3, NO_2, SR^4, OR^4, NR^4_2, OCR^4 (O), COR^4 (O), CR^4 (O), CNR^4_2 (O), aryl and substituted aryl;

R^4 is selected from aryl, substituted aryl, and substituted and unsubstituted branched or straight chain C_1 to C_6 alkyl; and

X is selected from Cl, Br and F; comprising reacting a benzothiadiazole of the formula



with S_8 at elevated temperature in a solvent inert to S_8 at a molar ratio of S_8 to benzothiadiazole of about 1:2 to 2:1.

15. A method according to Claim 14 wherein the solvent is selected from one or a mixture of decahydronaphthalene, nitrobenzene, dichlorobenzene, dimethylformamide, and dimethyl sulfoxide, and the temperature is about 140° to 200°C.

16. A method according to Claim 15 wherein the temperature is 160° to 190°C and the ratio of S_8 to benzothiazole is about 1:1.

17. A method according to Claim 14 conducted in the presence of 1,4-diazabicyclo[2.2.2]octane.

18. A method according to Claim 15 conducted in the presence of 1,4-diazabicyclo[2.2.2]octane.

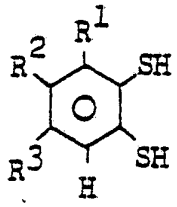
19. A method according to Claim 16 conducted in the presence of 1,4-diazabicyclo[2.2.2]octane.

20. A method according to Claim 17 wherein the ratio of 1,4-diazabicyclo[2.2.2]octane to benzothiadiazole is 0.1:1 to 2:1.

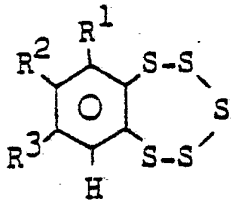
21. A method according to Claim 18 wherein the ratio of 1,4-diazabicyclo[2.2.2]octane to benzothiadiazole is 0.1:1 to 2:1.

22. A method according to Claim 19 wherein the ratio of 1,4-diazabicyclo[2.2.2]octane to benzothiadiazole is 0.1:1 to 2:1.

23. A method for making a 1,2-benzenedithiol of the formula



comprising reducing a benzopentathiepin of the formula



wherein

R^1, R^2 and R^3 are the same or different and are selected from H, X, CX_3, NO_2, SR_4, OR^4, NR^4_2, OCR^4 (O), COR^4 (O), CR^4 (O), CNR^4_2 (O), aryl and substituted aryl;

R^4 is selected from aryl, substituted aryl and substituted and unsubstituted branched or straight chain C_1 to C_6 alkyl; and

X is selected from Cl, Br and F.

24. A method according to Claim 23 wherein the reducing agent is selected from at least one member of the group sodium borohydride, lithium aluminum hydride, trialkyl phosphite, and zinc/aqueous acid, the reaction conducted in the presence of a solvent at about 0° to 60°C.

25. A method according to Claim 24 wherein the reducing agent is sodium borohydride and the ratio thereof to benzopentathiepin is from about 2:1 to 6:1.

26. A method according to Claim 24 wherein the reducing agent is lithium aluminum hydride and the ratio thereof to benzopentathiepin is from about 2:1 to 6:1.

27. An anti-fungal formulation comprising an effective amount of a compound according to Claim 1.

28. A formulation according to Claim 27 wherein the compound is 7-trifluoromethylbenzopentathiepin.

29. A formulation according to Claim 27 wherein the compound is 7-dimethylaminobenzopentathiepin.

30. A formulation according to Claim 27 wherein the compound is 7-methoxybenzopentathiepin.

31. A formulation according to Claim 27 wherein the compound is 6-trifluoromethylbenzopentathiepin.

32. An anti-viral formulation comprising an effective amount of a compound according to Claim 1.

33. A formulation according to Claim 32 wherein the compound is 7-dimethylaminobenzopentathiepin.

34. A plant disease control formulation comprising an effective amount of a compound according to Claim 1.

35. A compound according to Claim 1 wherein R^1 and R^2 are both NR^4_2 and R^3 is H.

36. A compound according to Claim 35 wherein R^4 is methyl.

37. A compound, 4,5-bis(dimethylamino)-1,2,3-benzothiadiazole.

INTERNATIONAL SEARCH REPORT

International Application No PCT/US84/00870

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [3]

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC[3] C07D 341/00, A01N 43/24, C07C 148/00

II. FIELDS SEARCHED

Minimum Documentation Searched [4]

Classification System	Classification Symbols		
U. S.	549/11 548/127	568/62, 63, 65, 66 564/162, 440 560/18, 106	562/142, 432 424/277

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [5]

Chemical Abstracts Volumes 1-100
Fieser et al., Reagents for Organic Synthesis Volumes 1-10.

III. DOCUMENTS CONSIDERED TO BE RELEVANT [14]

Category *	Citation of Document, [16] with indication, where appropriate, of the relevant passages [17]	Relevant to Claim No. [18]
X	N, Feher et al., Tetrahedron Letter 2125-26 (1971)	1-11, 35,36
X	N, Feher et al., Z. Naturforsch. 27b, 1006-7 (1972)	1-11. 35,36
X	US, A, 4,104,467, published 1 August 1978, Sprague et al.	12,13
X	N, Ward et al., J. Chemical Society, 1963, 4794-4803 (1963)	37
A	US, A, 4,094,985, published 13 June 1978, Vladuchick	27-34
A	N, Hunig et al., Liebigs Ann. Chem. 738, 192-4 (1970)	14-22
A	N, Krantz et al., J. Am. Chem. Soc. 103, 486-96 (1981)	14-22
A	N, Gassman et al., J.C.S. Chem. Comm., 1974 201-2 (1974)	23-26

* Special categories of cited documents: [15]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search [2]	Date of Mailing of this International Search Report [2]
8 August 1984	22 AUG 1984
International Searching Authority [1]	**Signature of Authorized Officer [20]**
ISA/US	

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

A	N, Overman et al., J. Am Chem. Soc. 98, 771-5 (1976)	23-26
X	N, Cairns et al., J. Am. Chem. Soc. 74,3982-8 (1952)	23-26
A	N, Harpp et al., J. Am. Chem. Soc. 104, 6045-53 (1982)	23-26
X	US, A, 3,686,329, 22 August 1972, Bernhart	23-26
X	US, A, 3,578,718, 11 May 1971, Schmidt	23-26

V. ☐ OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE [10]

This international search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1. ☐ Claim numbers....., because they relate to subject matter [12] not required to be searched by this Authority, namely:

2. ☐ Claim numbers....., because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out [13], specifically:

VI. ☒ OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING [11]

This International Searching Authority found multiple inventions in this international application as follows:

See Form PCT/ISA/206

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.

2. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:

3. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:

4. ☐ As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

☐ The additional search fees were accompanied by applicant's protest.

☒ No protest accompanied the payment of additional search fees.